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DISEASES OF THE NERVOUS SYSTEM

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DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Electroencephalogram and A Psychological Battery in the Diagnosis of Organic Psychoses

JAY B. COHN, M.D., G. A. STECKLER, B.A.,
W. S. TAKACS, B.S., and J. LORENZO, M.A.
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In 1946 the organic psychoses represented about 55% of all first admissions to state mental hospitals in the U.S.[17] In addition, a large proportion of mental patients requiring prolonged hospital care fall into this category. It is evident that a large part of the psychiatrist's time is devoted to the detection and treatment of organic psychoses. The detection of such disorders and the differentiation of them from functional psychoses are often quite difficult. In many cases the diagnosis of an organic psychosis cannot be confirmed or demonstrated even at autopsy. Frequently one is forced to rely upon a complete work-up during the patient's stay at the hospital, including the electroencephalogram and several of the widely used psychological tests for organic impairment. Because of the importance of organic psychoses and the clinical problem of detecting them we have undertaken a clinical study of the value of both electroencephalographic and psychological examinations in detecting an organic substratum.

The authors were interested in answering the following questions:

(1) What is the relative efficiency of psychological tests and electroencephalograms with respect to detection of organic changes? (2) What are the limiting factors and conditions for optimal diagnostic efficiency of the EEG? (3) How does the spontaneous EEG compare in diagnostic efficiency with EEG's obtained during sleep and during photic stimulation of the retina? (4) Is the detection of organicity made more efficient by combining the results of psychological examinations and EEG recordings?

The EEG literature contains many articles dealing with changes in specific types of organic psychoses. Walter[20] made an extensive survey. He concluded that the presence of alpha rhythm is dependent upon intact cortical neurones, especially the deep layers, and upon thalamo-cortical connections. Further, that focal delta activity occurs only in the presence of cortical dysfunction from toxic, inflammatory, or degenerative processes. Trowbridge[19] investigated 68 patients suspected of having non-focal neurological disorders. He concluded that slow activity is common in cases showing dilated ventricles. This idea was opposed by Levin and Greenblatt,[16] who studied EEG's in patients with both cortical atrophy and ventricular dilatation. Their results show that the EEG was often abnormal with cortical atrophy but not with cases of ventricular dilatation. Cases with clinical seizures, regardless of whether they had cortical atrophy or ventricular dilatation, had a high proportion of abnormal EEG's.

In an earlier paper[9] the last-named authors made an extensive comparison of the relative value of the EEG and abstraction tests in the diagnosis of brain damage. Their results of this investigation in 1945 have gone essentially unchallenged in the suc-

From Cleveland Receiving Hospital

ceeding years. They found only slight correlation between ratings on the two examinations. They felt that the abstraction tests were more valid than the EEG in diagnosing brain damage, but that the combined use of both tests "may give greater diagnostic validity." They pointed out that in cases with non-progressive or slowly progressive brain lesions, the EEG is often negative, despite clearly demonstrable brain pathology. Gibbs[5] has reported that sleep EEG's will show abnormalities not seen on spontaneous recording, particularly in cases with vascular lesions. In our sample, however, there were too few cases with vascular lesions, so that we have insufficient data bearing upon this matter. Weil[22] has shown the value of photic driving (photic EEG) in eliciting abnormal EEG's. We do not know of any paper in the literature dealing with the relative value of spontaneous, sleep and photic EEG's in the detection of organic psychoses in a large and heterogenous group of hospitalized patients, and this study is, in part, an attempt to fill that gap.

Although there is a great deal of psychological literature devoted to the diagnosis of organic damage by use of psychological tests, many of the articles deal only with single tests. Many other articles are essentially attempts to single out "signs" pathognomic of organicity. We agreed with Rashkis[18] and Hoedemaker and Murray[12] that greater diagnostic validity could be attained with a battery of tests covering a relatively wide range of thinking and behavior than with the relatively restricted coverage provided by a single test. We also felt that the "sign" or mechanical approach to psychological diagnosis does not usually yield very high validity, which opinion is shared by others; nor does it yield additional data (aside from classification with respect to organicity) which is often of value in treating patients. We felt that a combined quantitative and qualitative analysis of a battery of tests might yield high diagnostic validity.

One of the most general psychological criteria of organicity, is according to Goldstein and Scheerer,[7] the lack of the "abstract attitude" to a greater or lesser extent. Another basic criterion is loss of (not misuse of, as in functional disorders) various intellectual functions, especially those requiring new learning or the novel application of old techniques.[21] One other important criterion for organic damage is the disturbance of visuomotor functions.[3,8]

It is frequently difficult to distinguish functional disturbances of thought and behavior from organic disturbances. However, the overall pattern of behavior, plus characteristic types of errors and approaches to problems often provide the necessary clues enabling us to single out the cause of the difficulties in these doubtful cases.

METHOD AND PROCEDURE

Patients admitted were assigned at random to this study. The population of this hospital consists mainly of patients in the acute stage of a psychotic episode. All kinds of psychiatric entities are represented with the exception of the senile psychoses. We excluded from the study: (1) those patients who would be hospitalized less than 14 days; (2) patients who could or would not cooperate for testing; and (3) patients whose disease could not be classified as organic or non-organic accurately. Very few patients were excluded for these reasons. Every patient was given a complete work-up, consisting of:

1. Complete social history.
2. Mental status examination.
3. Complete physical examination.
4. Neurological examination.
5. Skull x-ray (not done for a few patients).
6. Blood analysis, including a complete blood count.
7. Complete urine analysis, including porphyrins.
8. Complete spinal fluid analysis.
9. Observation by skilled psychiatric personnel of the patient's ward behavior.
10. Specialized procedures as indicated, such as pneumoencephalograms and angiograms.

On the basis of these ten procedures, patients were divided into organic and functional (non-organic control) groups. While admittedly not a final grouping, it served as a working criterion against which both the EEG and psychological examinations were evaluated.

In evaluating the laboratory results in these patients, some of the findings seem worth mentioning. The results of the following studies were essentially non-contributory: urine, complete blood count, and urine porphyrins. It also seemed significant

that urine porphyrins were negative on 686 consecutive admissions at our hospital. On admission most of our patients showed a trace of glycosuria, acetonuria, and albuminuria. In all cases these were no longer present when re-checked during the hospital stay. In many cases where the blood serology was positive, the spinal fluid was not.

Three EEG records were obtained for each patient as soon after admission as possible. Both ear-scalp and scalp-scalp recordings were used with ten electrode placements including the reference electrodes. One recording was done with the patient awake (spontaneous EEG), a second was done while the patient was asleep (either natural sleep or sleep produced by administration of seconal), and the third was obtained while the patient was subjected to photic stimulation of the retina, gradually increased from 4 to 20 flashes per second.

A battery of four psychological tests was uniformly administered to each patient as soon after admission as possible. These tests were: the Bender-Gestalt Visual Motor Test,[3] the Graham-Kendall Memory for Designs Test,[9] the Wechsler-Bellevue Intelligence Scale for Adults Form I,[21] and the Rorschach Ink Blot Test.[15]

In order to quantify our measures of organic impairment, we rated the psychological scorings and EEG's on a 5 point scale. We found the criteria set forth by Greenblat, et al.,[9] suitable for our purposes. The psychological battery results were divided into five classes as follows:

CLASS 1: No impairment due to organicity.
CLASS 2: Probably no impairment.
CLASS 3: Questionable but tending to show some impairment.
CLASS 4: Definite impairment.
CLASS 5: Gross impairment.

Spontaneous EEG's were classified as follows:

CLASS 1: Normal frequency (8.5 to 12 per second). No significant changes of frequency or amplitude during overbreathing.
CLASS 2: Slightly irregular rhythm with predominantly normal frequencies. No marked changes in frequency or amplitude during overbreathing.
CLASS 3: Irregular tracings with mixed frequencies, with only occasional random slow or fast potentials. Slight to moderate change in frequency or amplitude in overbreathing.
CLASS 4: Considerable activity slower than 8.5 per second or faster than 12 per second, or a very mixed pattern with numerous abnormal waves. Overbreathing usually accompanied by a decrease in frequency and an increase in amplitude.
CLASS 5: Grossly abnormal frequency and irregularity with or without paroxysmal rhythmicity. Marked changes during overbreahing with gross effects often after only short periods of overbreathing.

Photic and sleep EEG's were classified as normal, borderline, and abnormal.

The criteria for classifying sleep records were as follows:

NORMAL: No asymmetry in frequency or amplitude; no seizure discharges; and no focal abnormality.
BORDERLINE: Rare or occasional bursts of irregular slow waves or minimal asymmetry in frequency or amplitude.
ABNORMAL: Frequency or voltage asymmetries; seizure discharges; focal abnormality.

We used the following criteria for classifying photic EEG's:

NORMAL: No frequency changes on photic frequency variations; no seizure discharges.
BORDERLINE: Minimal or occasional frequency changes with occasional seizure bursts on photic frequency variation.
ABNORMAL: Changes in frequency on photic frequency variations; seizure discharges; focal abnormality.

DESCRIPTION OF PSYCHOLOGICAL TESTS AND PROCEDURES

The four psychological tests were all administered and evaluated by the psychologist attached to the research project. A psychological report was written for each patient. Evaluation of the test protocols was global and qualitative as well as quantitative. The patient's behavior and verbalizations during the testing session were considered in each case. The general aim in this procedure was to duplicate conditions of test administration and interpretation which generally exist in clinical settings. There was, therefore, no attempt made to evaluate test protocols "blindly," i.e., without observing the patient during test administration. Tests were chosen on the basis of wide clinical usage and demonstrated utility in the evaluation of both organic and functional disorders.

Both the Bender-Gestalt test and the Graham-Kendall Memory for Designs test measure visuo-motor ability. In addition, the Graham-Kendall test measures immediate memory. Both tests consist of non-mean-

ingful designs which the patient is asked to copy (Bender-Gestalt) or draw from memory (Graham-Kendall). The authors' criteria[3,8] were considered in the final evaluation.

The Wechsler-Bellevue Intelligence Scale for Adults (Form I) is an individual test of intellectual functioning; it contains both verbal and performance scales. Results were evaluated in terms of intra-test variability,[2,21] and qualitative factors, particular attention being paid to the underlying processes implicit in a given response and the approach to a given problem by the patient.

The Rorschach Ink Blot Test is too well known to require description here. We used the Hertz[11] system of administration and scoring, and evaluated the results for organicity in light of criteria set forth by Klopfer and Kelley,[15] Hughes,[13] and Aita, Reitan and Ruth.[1]

SUBJECTS

We had 70 patients in our research sample, 35 in the organic group and 35 in the control (functional) group. The following tables indicate clinical diagnoses for the patients in each group.

TABLE I

Organic Psychoses	*No. of Cases*
General Paresis	11
Psychosis with Alcoholic Encephalopathy	11
Post-Traumatic Psychosis	7
Psychosis with Cerebral Arteriosclerosis	1
Psychosis with Cerebral Atrophy	3
Toxic Psychosis	2
	35

TABLE II

Non-Organic Syndromes	*No. of Cases*
Schizophrenia	21
Manic Depressive Psychosis	4
Involutional Psychosis	3
Psychoneurosis	6
Paranoid Condition	1
	35

The organic group contained 34 men and 1 woman; the mean age of the group was approximately 47 years. There were 15 men and 20 women in the functional group, the mean age of which was approximately 40 years. The age range for the entire sample was 20 to 68; the range for each group was similar.

RESULTS

Average Rating of Organic and Functional Groups on Each Test:

Fig. 1 depicts the average rating of both groups on the psychological and EEG tests. Here we see that on the average, the psychological examination diagnosed organicity with the greatest efficiency, i.e., the average organic patient was classified as organic, and the average functional patient was classified as non-organic. The three EEG's were much less efficient. The spontaneous and sleep procedures were somewhat better than the photic in this respect. On all three EEG's the average control or non-organic patient had an EEG record which, though it approached the organic range, still did not fall definitely under the heading of "abnormal." This poor diagnostic efficiency of the EEG's can be traced to the relative infrequency of definitely abnormal EEG's among our organic sample, and to the relative frequency of abnormal and borderline EEG's among our non-organics. On the spontaneous EEG, for example, only 25% of the organics were rated abnormal to grossly abnormal (class 4 & 5).

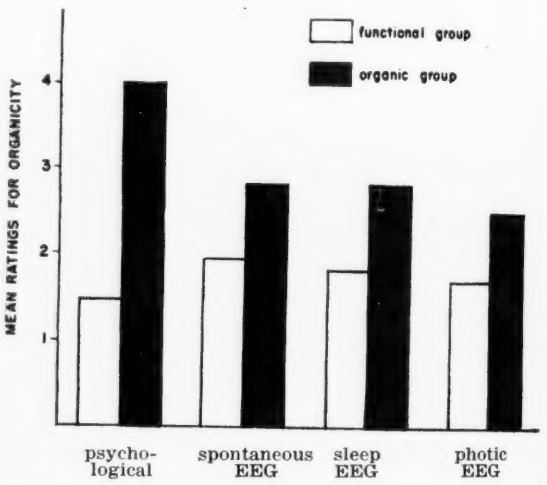

Fig. 1. Mean ratings for functional and organic groups on psychological tests and EEG's.

Fig. 2 will give the reader some idea of the extent of agreement with the criterion of the psychological tests and EEG's. Somewhat arbitrarily (although the distributions of ratings approached bimodality), we grouped ratings of 1 and 2 as indicative of

no organicity and ratings of 3 to 5 as indicative of organicity. From Fig. 2 it will be seen that the psychological battery had the greatest classificatory efficiency and the photic EEG the least. In other words, the psychological results "correctly" placed most organics within the organic group and most non-organics within the non-organic group. The spontaneous EEG had the next greatest discriminative power, but it picked up abnormalities in 37% of the non-organic group, or more than twice the reported percentage in the general population. A relatively lower percentage of the controls had abnormal photic and sleep records, but it will be seen that only half of the organics had abnormal records on these two procedures. In short, the percentages of all patients correctly classified according to the criterion (organic vs. non-organic) were:

PSYCHOLOGICAL BATTERY: 91% agreement with the diagnostic criterion.

SPONTANEOUS EEG: 66% agreement with the diagnostic criterion.

SLEEP EEG: 64% agreement with the diagnostic criterion:

PHOTIC EEG: 58% agreement with the diagnostic criterion.

If we had classified our sample purely by chance it is likely that 50% would have been correctly placed into organic and non-organic groups. It is obvious that the photic EEG in our sample of patients was not much better than a purely chance placement.

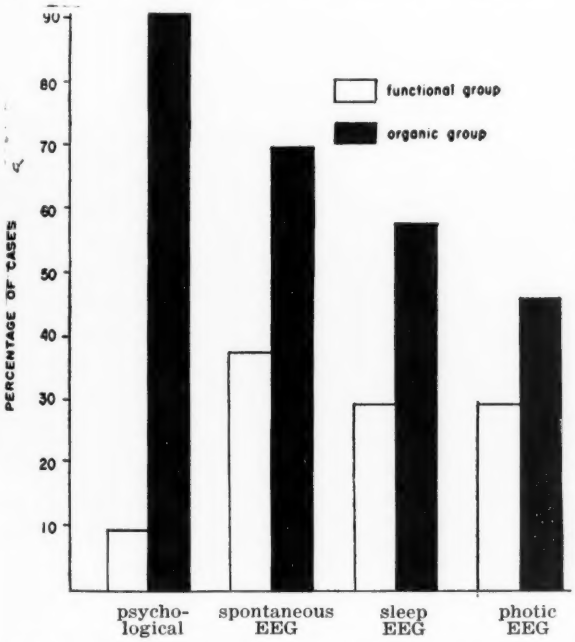

Fig. 2. Percentage of cases in functional and organic groups rated as borderline or worse with respect to organicity.

Combined Use of Psychological and EEG Evaluations in Predicting Organicity:

Following the suggestion of Greenblatt, et al.,[10] we analyzed the diagnostic validity of the psychological battery in combination with each of the three EEG's. These authors found that of those patients having abnormalities in both spontaneous EEG and abstraction tests, 91% were validly classified as organics. Our results are in substantial agreement with these findings. In fact, 95% and 93% of our cases with abnormal psychologicals and sleep and photic EEG's respectively, were validly classified as organic. These high figures are somewhat misleading.

We learn from Fig. 3 that the percent of organics with abnormalities in both psychologicals and EEG's is only 60%, 51%, and 37% for spontaneous, sleep, and photic EEG's respectively. It is true that in one sense, "dual" abnormality is highly indicative of organicity. However, when we attempt to pick out the organics from a heterogenous group of mental patients (as in our sample), we find that this method classifies as follows:

Abnormal psychological + abnormal spontaneous EEG: 77% agreement with criterion.

Abnormal psychological + abnormal sleep EEG: 74% agreement with criterion.

Abnormal psychological + abnormal photic EEG: 67% agreement with criterion.

Although this combined method improves the diagnostic validity of each of the EEG's it is not as efficient as the psychological battery by itself, which, as we have seen predicted with 91% accuracy the final diagnostic classification of the entire sample.

DISCUSSION

In our series the psychological battery was the most valid procedure in diagnosing the organics and in ruling out organicity in the non-organics. However, it is important to note that this series is heavily loaded with the long, chronic or slowly progressive organic psychoses. We had very few of the acute episodes seen in toxic and inflammatory diseases. Previous investigators[19,20] have confirmed the fact that the EEG is fre-

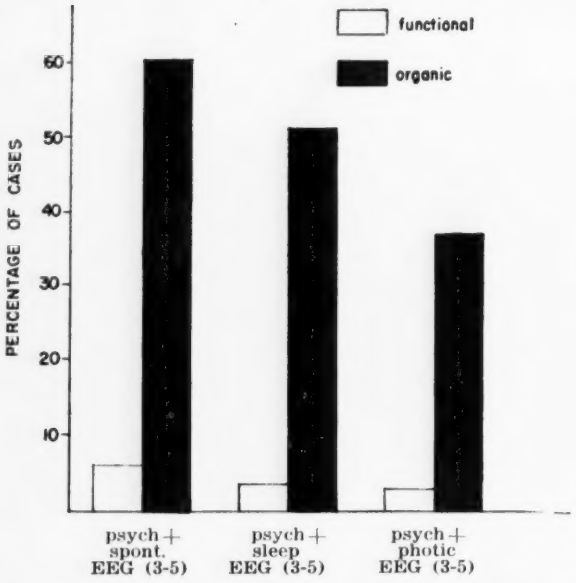

Fig. 3. Diagnostic efficiency of psychologicals in combination with each of three EEG's (spontaneous, sleep, and photic). Graph depicts percentage of cases in each group which were rated borderline or worse with respect to organicity.

quently negative in slowly progressive lesions. One might hypothesize that the transient and acute psychotic states so frequently seen in the general hospitals would have more EEG abnormalities. The argument of the relative values of EEG's in the awake and sleep states has been extensively documented in the literature. This controversy has centered about cases with focal brain pathology. Only one of our patients had a focal lesion. Hence our finding that spontaneous EEG's were better diagnostic aids must be limited to cases with organic psychoses unassociated with focal brain pathology.

The high percentage of abnormal EEG's in the control (functional) group needs some explanation. Various estimates of abnormal EEG's in supposedly normal people range from 10% to 14%.[4,6] Our abnormality of 37% in the control group on spontaneous EEG's is much higher. But our control group contained many patients who had chronic or recurrent functional psychoses. Of the 12 functional patients who had abnormal spontaneous EEG's, 8 had had at least one course of ECT prior to admission to the hospital. The possibility that the previous treatment left them with residual EEG abnormalities cannot be overlooked. It would appear that this is the most logical explanation for this relatively high figure.

The photic stimulation procedure is relatively new and has found extensive usage in provoking seizure discharges in the convulsive disorders. We have found no reference to its use in our type of cases. Photic stimulation had a poor discriminative value. On one of our post-traumatic cases it precipitated a clinical seizure despite the absence of seizure discharges in previous recordings. The photic stimulation EEG is a relatively simple and innocuous procedure and we found it of help in a few selected cases. Our high confirming scores with our psychological battery strengthened our belief in the efficiency of a wide range of tests using the integration patterns of the patient rather than simple signs as our criteria.

We did not establish the reliability of our psychological ratings. The very clinical nature of our procedure made this difficult. Attempting to establish inter-rater agreement on the basis of "blind" appraisal of test protocols alone would have been contrary to the aims of our procedure. A good amount of the patient's behavior and verbalizations cannot be captured in writing. Thus "blind" appraisal is apt to be less valid than clinical appraisal. There is an alternative method in establishing reliability, i.e., to have two or more psychologists present during the actual testing sessions, and then to compare their ratings on the organicity scale. Because of time limitations and personnel shortage, we were unable to do this. We do, however, have one kind of information which we feel sheds light on the reliability of our ratings. We compared the validity of the psychological ratings made by our project psychologist on the last forty-three cases in the sample with the combined validity of the psychological ratings made on the first twenty-seven cases by two other psychologists. The validities for each segment of the sample (where ratings of one and two were considered normal and three to five as abnormal) were quite similar. On this basis we believe that the high validity of our psychological battery can be duplicated by any psychologist with comparable training and experience.

Our results in cases of general paresis con-

firm the previous reports in the literature. Many cases of severe paresis have little abnormality in the EEG. One of our most severe cases died and was autopsied. His meninges showed severe changes but his cortex showed almost normal structure. It is not surprising then that his sleep and photic EEG's were within normal limits, since there was little demonstrable involvement of the parenchyma. This example would tend to confirm Walter's[20] conclusion that the alpha rhythm is dependent on intact neuronal structure. This implies that involvement of other structures would correlate poorly with the EEG, which was true in this case. This is probably the best explanation for the normal EEG's in some of our paretics. In our post-traumatic cases the EEG's predicted poorly. Only one had a clinical seizure and that was on photic stimulation. This in itself may explain the poor correlation here. Another factor that seems important is that all our post-traumatic cases came to us many weeks after their injury. This in many cases was probably long enough for their EEG's to return to normal or borderline status.

We strongly recommend that the psychological battery and a single EEG be given to every psychotic patient in whom the diagnosis is uncertain or the course atypical. These borderline cases can more correctly be diagnosed with the aid of these tests. There are no substitutes for the accepted clinical workup but when used as laboratory procedures they are of definite value in detecting which psychotic patients have organic disorders as their etiological factor.

In regard to the individual tests making up the psychological battery, we found the Rorschach and the Wechsler-Bellevue to be the most efficient in establishing or ruling out the presence of organicity. The Bender-Gestalt and the Graham-Kendall were less useful, the latter test helping least of all. The relative diagnostic superiority of the Rorschach and the Wechsler-Bellevue can probably be explained quite simply: both of these tests are much more comprehensive than either the Bender-Gestalt or the Graham-Kendall. We found that the Graham-Kendall did not distinguish well between functional and organic patients especially when only the quantitative score was considered. This was because many of the functional patients were preoccupied, affecting their ability to attend to or remember the designs after brief presentation. It is assumed that in those cases where the psychological evaluation disagreed with the clinical diagnosis the discrepancy could in most instances be traced in ambiguity or sparseness of psychological test data.

SUMMARY

We administered spontaneous, sleep and photic EEG's plus a psychological battery to seventy hospitalized psychiatric patients. One half of these were classified as organic psychoses on clinical grounds. The remainder were cases of functional disorders and were used as controls. Our studies indicate that our psychological battery was the best detector of organicity; the EEG in the non-sleep state was second best.

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Evaluation of Repeated Courses of Electroconvulsive Therapy in Chronic Schizophrenia

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Introduction

The purpose of this study is to evaluate the effects of repeated courses of electroconvulsive therapy (ECT) on patients with chronic mental illness, most of whom are schizophrenic. A total of 1, 128 patients received electrotherapy and/or insulin therapy at this hospital from 1943 to 1951. From observations of patients it is the writer's impression that if a patient did not respond favorably to the last course of ECT, further therapy of this kind was of little value. The practical aspects of this finding would be to spare the patient further treatment and leave more time for the personnel to devote to the patients' individual needs. It is not uncommon for patients without benefit from previous courses of ECT, to be given another course of treatment in the hope that it might bring improvement. *Literature*—Despite the great wealth of literature on ECT, there is relatively little specific information on the value of repeated courses of treatment in chronic schizophrenia. There is question as to what constitutes an adequate course but it is generally agreed that 15 to 20 grand mals is usually sufficient. Danziger *et al.*[1] favored 25 grand mals as a reasonable number of treatments since they found that 50 to 77 percent of recoveries occurred by the fifteenth and twentieth treatment respectively. However, this occurred in patients whose duration of illness was six months or less. Atkin[2] thought that if there were any improvement it would be noticed by the twelfth convulsion. Lowinger and Huddleson[3] believed that the incidence of improvement was greater in those receiving from 16 to 20 grand mals per course. Malzberg[4] found that better results were obtained in those patients who had 15 convulsions or less than in those who had more convulsions. This apparent discrepancy may be reconciled upon the basis that the affective or schizoaffective disorders have a better prognosis and respond with fewer treatments than the more malignant schizophrenic disorders. Palmer *et al.*[5] found that the patient who showed marked improvement did so with a

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significantly lower number of treatments than those with poorer results. In MacKinnon's[6] series of 300 patients of all types the number of grand mals rarely exceeded 15 except in those who tended to relapse. Bennett[7] found that six treatments were usually sufficient in the schizo-affective disorders and in a personal communication stated that if the patient did not respond early in the treatment he would be unlikely to benefit from later therapy. Kalinowsky[8,9] considered 20 grand mals to be adequate for a course and in a personal communication stated that if favorable response to treatment occurred it was generally early in the course. Martin[10] averaged 20 grand mals for the catatonic and hebephrenic types and ten grand mals for others.

The usual number of treatments per week were generally noted as two to three by Spiegel,[11] Bellak,[12] and Kalinowsky.[13] There has been a trend by some writers[14,15,16] to increase the frequency of treatment in order to create a confused and regressed state which was believed to enhance the value of therapy in certain disorders. Kalinowsky *et al.*[17] believed that confusion was not necessary. Alexander[18] stated that 30 days in the post-treatment period were sufficient to permit the appearance of any favorable alterations which may occur.

Method

The first group studied consisted of 164 patients, all males, between the ages of 21 and 63 years at the time of therapy (Table 1). The duration of illness was over two years and with few exceptions the patients were classified as chronic schizophrenic reaction of various types. The results of treatment seemed to fall into four main categories:

I. The first category was made up of patients who did not show any essentially sustained improvement with first or subsequent courses of ECT.

II. The second category was made up of patients who did not show any essentially sustained improvement with the last course but did show improvement in subsequent courses of ECT.

III. The third category was made up of patients who showed improvement in early courses but failed to improve on subsequent courses of ECT.

IV. The fourth category was made up of patients showing improvement on first and subsequent courses of ECT.

TABLE 1

RESULTS OF ECT IN FIRST GROUP

Categories	First: Number of Grand Mals	First: Number of Patients	Additional: Total Number of Courses	Additional: Average Number of Courses per Patient	Additional: Total Number of Grand Mals	Additional: Average Number of Grand Mals per Course
	1 — 10	12	7	0.6	136	19.4
I	11 — 15	36	37	1.0	653	17.8
	16 — 20	52	47	0.9	885	18.8
	1 — 10	0	0	0	0	0
II	11 — 15	0	0	0	0	0
	16 — 20	0	0	0	0	0
	1 — 10	12	11	0.9	118	10.7
III	11 — 15	9	13	1.4	215	16.5
	16 — 20	10	25	2.5	359	14.4
	1 — 10	12	15	1.3	230	15.3
IV	11 — 15	11	11	1.0	144	13.1
	16 — 20	10	8	0.8	171	21.4
	Total	164	174	1.1	2,911	16.7

There were no patients in the second category indicating that none of these patients improved with further ECT if they had failed to benefit from the preceeding course of treatment. Since all these patients were on the acute and subacute continued treatment services, it is obvious that they had poor results from active treatment. Those who improved on early and subsequent treatments (Category IV) relapsed later.

It was considered that any benefit resulting directly from ECT would show itself within the first month after the termination of the treatment, and any changes which occurred after this period were regarded in the nature of the variation of mental illness. When the improvement was maintained for over one month, it was regarded as a relatively sustained response but if less than one month it was regarded as temporary. Of course, any evaluation of the patient's response is necessarily subject to the same criticisms inherent in all clinical impressions, but in most instances the results were arrived at by two psychiatrists, supple-

mented by daily observation and reports from ancillary personnel. The temporary responses have not been included in this study but have been noted in the records for prognostic factors if the patients were considered for leukotomy.

Since it is obvious that the first group of 164 patients by virtue of the end results did not respond favorably to ECT, a study was made of the 238 additional patients who had multiple courses of ECT. The diagnoses in this second group were schizophrenic reaction of various types in about 90 per cent of the patients. The age, duration of illness, and sex were approximately similar to the first group. Both series were given treatments on an average of two to three grand mals a week with a varied number of treatments per course. The average number of grand mals per course for both groups was about 15. The results of the second group have been noted in Table 2, 3 and 4.

TABLE 2

RESULTS OF ECT IN SECOND GROUP

COURSES OF ECT

Categories	First: Number of Grand Mals	First: Number of Patients	Additional: Total Number of Courses	Additional: Average Number of Courses per Patient	Additional: Total Number of Grand Mals	Additional: Average Number of Grand Mals per Course
	1 — 10	9	11	1.2	131	12.0
I	11 — 15	21	27	1.4	390	14.4
	16 — 20	35	52	1.5	839	16.0
	1 — 10	0	0	0	0	0
II	11 — 15	0	0	0	0	0
	16 — 20	4	7	1.8	81	11.6
	1 — 10	15	32	2.1	452	14.1
III	11 — 15	8	8	1.0	144	18.0
	16 — 20	24	36	1.5	570	15.8
	1 — 10	46	83	1.8	968	11.7
IV	11 — 15	31	62	2.0	1,145	18.5
	16 — 20	45	101	2.2	1,579	15.6
	Total	238	419	1.8	6,299	15.0

TABLE 3

RELATION OF CATEGORIES TO DIAGNOSES IN SECOND GROUP

Categories	Schizophrenic Reaction: Catatonic	Hebephrenic	Mixed	Paranoid	Simple	Affective Disorders	Others	Total
I	5	24	16	17	0	3	0	65
II	0	0	2	2	0	0	0	4
III	14	8	7	15	1	1	1	47
IV	18	14	32	34	1	22	1	122
Total	37	46	57	68	2	26	2	238

TABLE 4

RELATION OF CATEGORIES TO STATUS IN SECOND GROUP

Categories	Service: Discharged*	Privileged	Acute or Subacute	Continued Treatment	Total
I	9	8	20	28	65
II	3	0	0	1	4
III	12	8	12	13	47
IV	66	29	16	11	122
Total	90	45	48	55	238

*Includes five patients on trial visit (one by transfer to another hospital, and four by death).

The first group of 164 patients tended to confirm the impression that if a patient failed to show improvement with the first or previous course of ECT, he would be unlikely to benefit by further electrotherapy. The findings in the second group of 238 patients also tended to confirm this impression since there were only four patients who appeared to be exceptions. However, two of these patients had chronic alcoholism with psychotic reaction as complicating factors, one was cyclic in course and the fourth had been improving spontaneously when he received a short course of ECT which may have accelerated his improvement.

As seen in Table 2, the patients in category I did no better when they received more than 15 grand mals in the first course or subsequent repeated courses than they did with a lesser number of treatments. This does not refute the fact that some patients with chronic schizophrenic disorders do benefit to a varying degree on ECT and should receive treatment consistent with their response. It is not believed that the number of grand mals per course or the number of courses be pre-determined but the treatment should be tailored to the individual patient. Patients with affective or schizo-affective states generally require fewer treatments and have better response than those patients with predominantly schizophrenic symptoms. The writer agrees with Martin[10] that the

therapist usually recognizes which patient is showing improvement. If amelioration of symptoms is not noted by the fifteenth grand mal, it is quite unlikely that further therapy will cause much change.

It should be noted that there were nine patients classified as discharged in category I. This included five patients on trial visits (one by transfer to another hospital and four by death, not due to ECT). There were also eight patients on the privileged ward. These apparent inconsistencies may be understood when it is realized that these patients were not severely ill and were either taken home by their relatives because the patients were unhappy in the hospital or were able to adjust on an open ward level.

Summary

1. 1,128 patients received electro and/or insulin therapy between 1943 and 1951.

2. The first group consisted of 164 patients who were currently residing on the acute or subacute services. None of these patients showed improvement to subsequent electrotherapy after failure to improve on the previous course (category II).

3. Only four of the 238 patients in the second group apparently could be classified in category II.

4. Of the 238 patients, 122 (51 per cent) improved with the first and subsequent courses of ECT (category IV) and 47 (16 per cent) showed some improve on subsequent courses of ECT (category III).

5. The 100 patients in the second group who failed to respond to the first and subsequent courses of ECT (category I) did no better when the number of grand mals per course were 16 to 20 than with a lesser number.

Conclusions

1. Patients suffering from chronic schizophrenia do not respond favorably to further ECT if the previous course consisting of 16 to 20 grand mals given at the rate of two to three times a week were without noted benefit to the patient.

2. If a patient does not respond favorably in the first 15 grand mals, he is not likely to improve with more treatments.

Author's Note: The foregoing article was reviewed in the Veterans Administration and is published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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The Hair Whorl Sign for Handedness

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The problem of handedness in relation to dextrality and sinistrality has been open to much controversy. Theories of its causation are manifold, such as, heredity, gravitation, the origin of the subclavian arteries, unequal cerebral blood supply, the predominance of the larger bones of one side of the body, ocular dominance, cerebral dominance, and also theories in relation to environmental and cultural factors, all so well discussed by Blau[1] and also by Wile.[2] As yet there are no definite clinical studies to point to any anatomical basis for handedness. Anatomically, Newman[3] finds no relationship to handedness in the incidence of clock-wise and counter clock-wise hair whorls or in finger print patterns.

One of us (J.G.), a pediatrician, has been employing the hair whorl sign to recognize congenital handedness for the past 10 years. We have been unable to find such clinical description in the medical literature. We have concluded that congenital handedness can be recognized clinically by the hair whorl sign.

The hair whorl sign is a spot on the occipital region of the scalp where the hair begins to curve in a clock-wise or counter clock-wise (vast majority clock-wise) direction. The location of the spot is judged in relation to the sagittal suture. The sagittal suture can be recognized in the new born by palpation in the midline between the anterior and posterior fontanelles. It is not safe to judge location by mere inspection as the slightest flattening of one side of the skull gives a false impression. The same method is employed in adults but requires more care, the sagittal suture being felt as a slight elevation in the midline separating the parietal bones. The hair whorl may be located to the right (Fig. 1) or to the left (Fig. 2) of the sagittal suture, or at the mid-line (Fig. 3), or on both sides of the mid-line, but not necessarily equidistant (Fig. 4). If the hair whorl is to the left of the mid-line (left hemisphere), the subject is congenitally right handed; if the hair whorl is to the right of the mid-line (right hemisphere), the subject is congenitally left handed; if the hair whorl is in the mid-line, the subject is considered to be congenitally ambilateral; if there are two hair whorls, the subject is considered to be congenitally ambidextrous. For clarity, ambidexterity is defined as the capacity to use both hands well and with equal facility; ambilaterality is defined as the ability to use both hands equally but with no definite skillful ability in either hand. One whorl may be well defined while another may be covered by the hair in such manner that it cannot be seen unless the hair is brushed aside to the other side of the head. When there are two whorls they are usually located on opposite sides of the scalp, although we have seen two cases with both whorls on the same side of the scalp. When there are two whorls they may be as little as a quarter of an inch apart, although usually the distance is greater. The single whorl is usually clock-wise whereas in a double whorl the one on the left side of the head is usually clock-wise and the one on the right side is usually counter clock-wise. If it is difficult to palpate the sagittal suture the external protuberance of the occipital bone can be used as a landmark to determine whether the hair whorl is to the right, left, or mid-line. The hair whorl sign cannot be employed in bald people, or in either sex with kinky hair and it is found with difficulty in women with long hair.

The problem of handedness is complicated by the fact that people are neither 100 per cent completely right handed nor left handed. Therefore, in order to confirm the validity of the hair whorl sign, we have employed a number of subjective and objective tests, a modification of those employed by Hull[4] and Blau.[1] Eight hundred and sixteen patients were studied from birth to determine

From the Neuropsychiatric Service and Pediatric Service, Fordham Hospital, Bronx, New York.

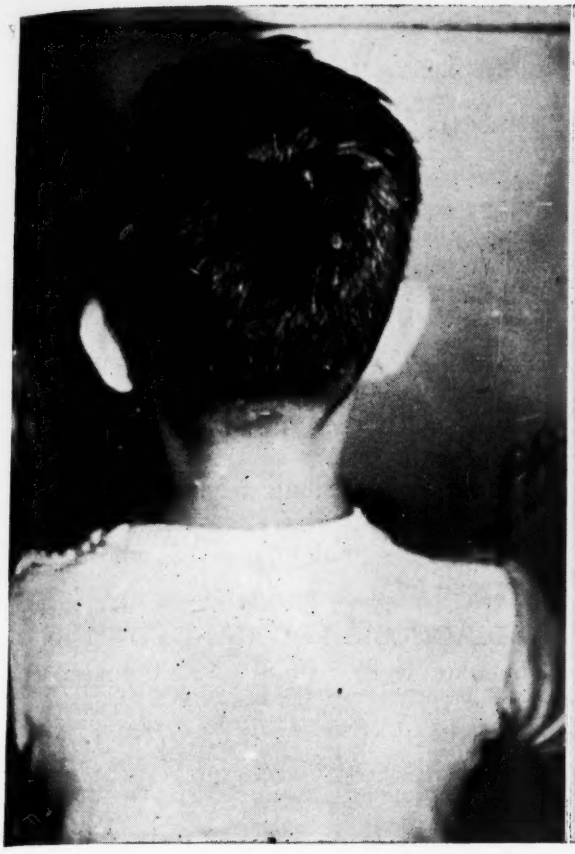

Fig. 1. Right hair whorl. (Congenital left handedness.)

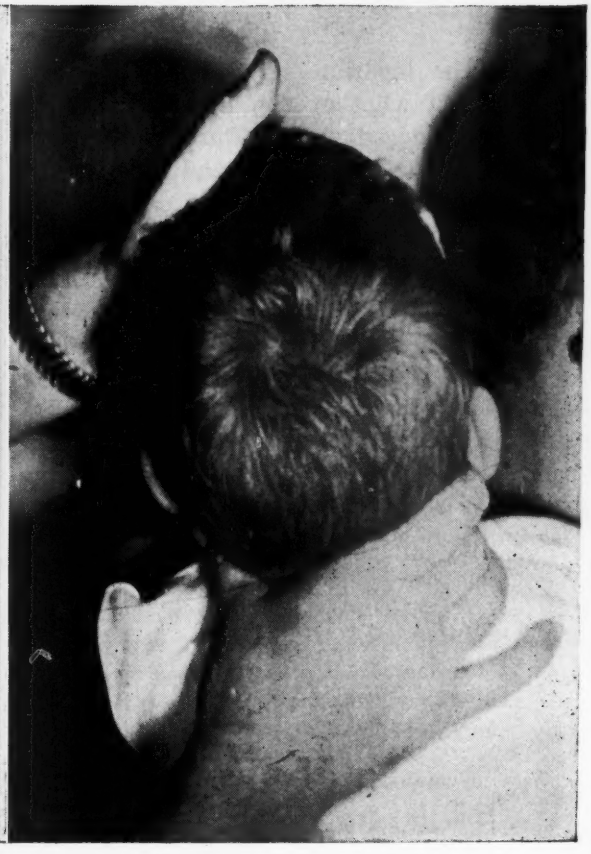

Fig. 2. Left hair whorl. (Congenital right handedness.)

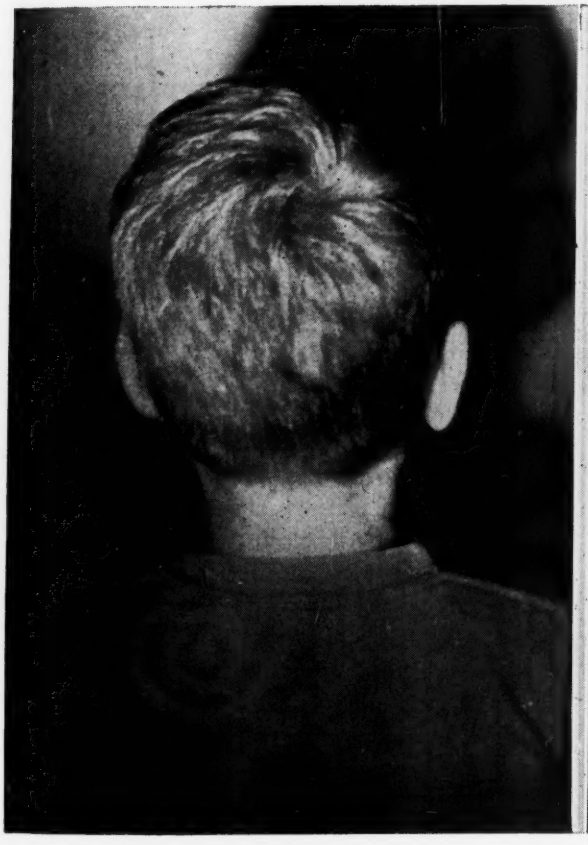

Fig. 3. Mid-line hair whorl. (Congenital ambilaterality.)

Fig. 4. Double hair whorl. (Congenital ambidexterity.)

whether the location of the hair whorl changes and whether the hair whorl sign can be considered valid. Furthermore, we have also tested 250 male and 250 female subjects from Fordham Hospital, ranging in age from 5 to 70 years.

The study of the subjects at Fordham Hospital included patients, physicians, nurses, and attendants. After it was determined by the hair whorl sign whether the subject was congenitally left or right handed, ambilateral or ambidextrous, they were given subjective tests in the form of questions, as well as objective tests.

For the males the following questions were asked:

1. Which hand holds a hammer?
2. Which hand deals cards?
3. Which hand holds a handkerchief?
4. Which hand waves good-bye?
5. Which hand winds a watch?
6. Which hand holds a tooth brush?
7. Which hand holds a spoon?
8. Which hand holds a comb?
9. Which hand is used in writing?
10. Which hand holds a knife?
11. Which hand throws a ball?
12. Over which shoulder is a bat held?
13. Which hand puts key into the lock?

The answers to these questions were tabulated as right, left, or the use of both hands.

There were 6 objective tests for handedness.

1. Cross legs. Which leg was on top? If the right leg was on top, it was considered a sign of dextrality (right handedness). If the left leg was on top, it was considered a sign of sinistrality (left handedness).

2. Clapping hands. Which hand was on top? If the right hand was on top or was the dominant hand in movement, it was considered a sign of dextrality. If the left hand was on top or was the dominant hand in clapping, it was considered a sign of sinistrality.

3. Clasping hands. Which thumb was on top? If the right thumb was on top, it was considered a sign of dextrality. If the left thumb was on top, it was considered a sign of sinistrality.

4. Look at book of paper matches. Note which side used. If the right side was used, it was considered a sign of dextrality. If the left side was used, it was considered a sign of sinistrality.

5. Strike a match. Which hand used? If the right hand was used, it was considered a sign of dextrality. If the left hand was used, it was considered a sign of sinistrality.

6. Eye Aiming Test. The subject extended his index finger and aimed at a small object at least 6 feet away. He then closed the right eye with the left eye open and if the finger moved to the right of the object, the subject was considered to have right eye dominance (a sign of dextrality). If on closing the left eye with the right eye open and the finger moved to the left of the object, the subject was considered to have left eye dominance (a sign of sinistrality).

Analysis of Data: Table I. The hair whorl sign showed that of the 250 male subjects, 175 were considered to be congenitally right handed (left hair whorl), 53 congenitally left handed (right hair whorl), 15 congenitally ambilateral (mid-line hair whorl), 7 congenitally ambidextrous (2 whorls, one right, one left).

DIAGNOSIS FOR HANDEDNESS

	BY HAIR WHORL SIGN (Congenital Handedness)		BY SUBJECTIVE AND OBJECTIVE TESTS			
			Right		Left	
RIGHT	No.	%	No.	%	No.	%
(Left hair whorl)	175	70	171	98	4	2
LEFT						
(Right hair whorl)	53	21	31	58	22	42
AMBILATERAL						
Mid-line hair whorl)	15	6	14	93	1	7
AMBIDEXTROUS						
(Double hair whorl)	7	3	7	100	—	—
TOTAL	250	100%	Total	89% Right		
				11% Left		

TABLE I: MALE—RESULTS OF HAIR WHORL SIGN (CONGENITAL HANDEDNESS) AS COMPARED TO RESULTS OF HANDEDNESS BY SUBJECTIVE AND OBJECTIVE TESTS.

Of the 175 who were considered congenitally right handed, employing the above mentioned subjective and objective tests, it was found that in 42 subjects, all tests showed right handedness. Fifteen subjects employed either hand in one or more of the following subjective tests: holding a hammer, dealing cards, holding a handkerchief, waving good-bye, holding a tooth brush, holding a spoon, holding a comb, and throwing a ball. Sixty subjects were considered left handed on only one objective test; in the other objective tests they were considered right handed. In one subject either thumb was on top when the hand clasping test was repeated. In 41 subjects, the left leg was on top when crossing legs; in 65 subjects the

left hand was on top or the dominant hand in clapping; in 57 subjects the left thumb was on top in clasping hands. The left side of the match box was used by 2 subjects; both sides of the match box were used by 1 subject; one subject struck the match box with the left hand. In 13 subjects the object did not move in the aiming test; in 20 subjects the master eye was left. One hundred and twenty-nine subjects were considered to be right handed as the subjective tests were mainly right and three or more of the objective tests were right. We considered one congenitally right handed subject to be left as four of the six objective tests were left, namely crossing the legs, clasping hands, left side of the match box used, and the dominant eye left, and this same subject employed either hand in waving good-bye and holding a handkerchief. A twelve-year old subject showed all objective tests as left and 9 of the subjective tests as left. He considered himself left handed as he wrote with his left hand. He was closely associated with an uncle who was left handed. Scheidemann and Colyer[5] reported that a number of right handed second grade children were using their left hand in writing as these children were imitating their left handed teachers. Another subject was considered left handed as he employed either hand in waving good-bye, striking a match, and winding a watch, and three of the objective tests were left, that is, crossing the legs, clasping and clapping the hands. A nine-year-old subject was considered left-handed as only the aiming and clasping hands' tests were right, whereas all the other tests were left. Thus 4 of the individuals who were considered congenitally right handed according to the hair whorl sign were considered left handed according to the subjective and objective tests.

Of the 250 male subjects tested, 53 according to the hair whorl sign were congenitally left handed. Nine of these subjects showed all tests to be left. Twenty-two subjects were considered to be left handed as their subjective tests were mainly left and they showed three or more left handed objective tests. Twenty-two subjects were considered right, four of whom showed all subjective and objective tests to be right. If three or more of the objective tests were right, the subjects were considered to be right handed. Four individuals used the left hand in waving good-bye, holding a tooth brush, striking a match, and holding a spoon; one wrote with his left hand. It is interesting to note that 22 of these congenitally left handed subjects who were considered right handed by subjective and objective tests, claimed they were right handed.

Of the 15 subjects whose hair whorl was in the mid-line, one subject was considered to be left handed, and 14 were considered to be right handed from the subjective and objective tests. Five of these right handed individuals employed either hand in from one to six tests, such as, holding a handkerchief, a tooth brush, a bat, a spoon, waving good-bye, and dealing cards. Only one subject showed all subjective and objective tests to be right, whereas the others showed one or two objective tests to be left.

The seven subjects who showed a double hair whorl sign, one left and one right, were all considered to be right handed individuals from the subjective and objective tests. Two subjects showed all tests to be right. Five subjects had all their subjective tests right, but one or two of the objective tests were left, and therefore, these individuals were considered to be right handed.

For the female the following subjective tests were employed:

1. Which hand uses a can opener?
2. Which hand holds the scissors?
3. Which hand deals cards?
4. Which hand holds a handkerchief?
5. Which hand waves good-bye?
6. Which hand winds a watch?
7. Which hand holds a toothbrush?
8. Which hand directs the thread through a needle?
9. Which hand holds a spoon?
10. Which hand holds a comb?
11. Which hand is used for writing?
12. Which hand holds a knife?
13. Which hand throws a ball?
14. Which hand puts a key into the lock?

The answers to these questions were tabulated as right, left, or the use of both hands.

Five objective tests were employed for handedness, namely:

(1) clapping hands, (2) clasping hands, (3) striking a match, (4) look at book of paper matches, note which side is used, and (5) the eye aiming test.

Analysis of Data: Table II. The hair whorl sign showed that of the 250 female subjects tested, 191 were considered to be congenitally right handed (left hair whorl), 34 congenitally left handed (right hair whorl), 23 congenitally ambilateral (mid-line hair whorl), and 2 congenitally ambidextrous (2 whorls, one right, one left).

DIAGNOSIS FOR HANDEDNESS

BY HAIR WHORL SIGN (Congenital Handedness)			BY SUBJECTIVE AND OBJECTIVE TESTS			
			Right		Left	
RIGHT	No.	%	No.	%	No.	%
(Left hair whorl)	191	76	188	98	3	2
LEFT						
(Right hair whorl)	34	14	19	56	15	44
AMBILATERAL						
(Mid-line hair whorl)	23	9	23	100	—	—
AMBIDEXTROUS						
(Double hair whorl)	2	1	2	100	—	—
TOTAL	250	100%	Total	93%	Right	
				7%	Left	

TABLE II—RESULTS OF HAIR WHORL SIGN (CONGENITAL HANDEDNESS) AS COMPARED TO RESULTS OF HANDEDNESS BY SUBJECTIVE AND OBJECTIVE TESTS.

Of the 191 subjects who were considered congenitally right handed, employing subjective and objective tests, 63 subjects showed all tests to be right. In 10 other subjects classified as right handed, the subjects employed either hand in one or more of the following subjective tests: holding a handkerchief, waving good-bye, holding a spoon, holding a fork, holding a comb, throwing a ball, using scissors, holding a tooth brush, and dealing cards. Ten subjects used their left hand in one or more of the following subjective tests: dealing cards, winding a watch, holding a toothbrush, a can opener, a knife and scissors. Ninety-seven subjects showed left handedness on only one subjective test and in the other tests showed right handedness. Twenty-eight subjects showed left handedness on two objective tests. In 28 subjects the left hand was on top or the dominant hand in clapping. In 74 subjects, the left thumb was on top in clasping hands. Five subjects used the left side of book of matches or struck matches using left hand. In 15 subjects the dominant eye was left. In 22 subjects the finger did not move in the aiming test and in one subject the finger moved when either eye was closed. One hundred twenty-five subjects were considered to be right handed as their subjective tests were mainly right and they showed three or more objective tests to be right. Three subjects who were considered right handed, according to the hair whorl sign, were shown to be left handed according to subjective and objective tests. One of these subjects used her right hand in winding a watch, striking a match, and the dominant eye was right, but all the other tests were left. The two other subjects were considered to be left handed because three objective tests (clapping hands, clasping hands, and aiming tests) were left handed. Of these three subjects only one could explain the left handedness. A 20 year old student nurse stated she decided to become left handed; the reason for this cultural negativism could not be ascertained.

Of the 250 female subjects tested, 34 were considered to be left handed according to the hair whorl sign. Nineteen subjects were considered to be right handed by subjective and objective tests. Four subjects showed all objective and subjective tests to be right. Fifteen subjects were considered to be right handed as practically all the subjective tests were right and three or more of the objective tests were right. Four individuals used either hand in four to thirteen subjective tests, but all of them only used the right hand in writing. One subject still employed her left hand in directing a thread through a needle, but all the other subjective tests were right handed. This subject stated that she was left handed as a child but learned to become right handed. One subject held a handkerchief in the left hand but the other subjective tests were right. Fifteen subjects were considered to be left handed. One of these subjects employed either hand in dealing cards and threading a needle and used the right hand in waving good-bye, winding a watch, holding a spoon and writing; all the other subjective tests were done with

the left hand. Two subjects used the right hand in threading a needle and one subject used the right hand in winding a watch and putting a key into keyhole, but all the other subjective tests were done with the left hand. In all these individuals three or more of the objective tests were considered to be left.

Of the 23 subjects whose hair whorl was in the mid-line, six subjects showed all subjective and objective tests to be right. One subject used either hand in waving good bye, holding a spoon, a tooth brush, and threading a needle. Ten subjects were considered to be left handed in one objective test and seven were considered to be left handed in two objective tests. Thus, 17 of the subjects were also considered to be right handed as the majority of the subjective tests were right and three or more objective tests were also right.

Of the 250 female subjects tested, two showed a double hair whorl. In one subject either hand was employed to hold a handkerchief, and the left hand directed the thread through a needle; in clasping hands the left thumb was on top; in the aiming test the object did not move; all the other objective and subjective tests were right. In the other subject the left thumb was on top in clasping hands and all the other tests were right. Thus these 2 subjects were considered to be right handed.

Discussion

It can be argued that the hair whorl sign is invalid as the vast majority of the population is right handed and that the relative incidence of dextrality or sinistrality is not fixed but varies according to the tests employed. In the 250 male subjects, according to subjective and objective tests, 89 per cent were considered right handed and 11 per cent were considered left handed; in the 250 female subjects, according to subjective and objective tests, 93 per cent were considered right handed and 7 per cent were considered left handed. Furthermore, from our data it is noted that a large number of the subjects were neither completely right nor left handed. Blau states that in thumb crossing the division is about fifty, fifty; in eyedness for sighting 70 per cent right, and 90 per cent right for writing. It is also known that the more specialized and differentiated an activity, the greater the proportional incidence of dextrality. However, from our study it is shown that in the 250 males, four out of 175 subjects who were right handed according to the hair whorl sign were considered to be left handed according to subjective and objective tests, and of 53 male subjects who were considered to be left handed according to the hair whorl sign, 31 were right handed by subjective and objective tests. For the females, of the 191 subjects who were considered to be right handed according to the hair whorl sign, three were considered left handed by subjective and objective tests, and of the 34 female subjects who were considered to be left handed by the hair whorl sign, 19 subjects were considered to be right handed by subjective and objective tests. Therefore, taking the hair whorl sign on the one hand and considering the difference in results on the subjective and objective tests, it can be stated that there is a considerable degree of error. However, by scrutinizing the figures more closely, the margin of error in the considered congenitally right handed males was only 2 per cent and for the considered congenitally right handed females, the margin of error was also 2 per cent. The margin of error for the congenitally left handed males was 58 per cent, and for the congenitally left handed females 56 per cent. Furthermore, for the congenitally ambidextrous or congenitally ambilateral, the margin of error appeared to be 100 per cent, although a definite tendency towards ambilaterality or ambidexterity was noted. (Tables I and II.) How can this seeming error be explained? Blau claims that preference for the right side is a cultural and social convention and that the incidence of dextrality gradually increases in children with age as they are exposed to more and more educational and cultural influences. Our figures would then appear to be correct and prove that the hair whorl sign is valid, for the margin of error is practically negligible for the congenitally right handed individuals, whereas the margin of error is considerable for the congenitally left handed, congenitally ambidextrous, or congenitally ambilateral

adult individuals. In our male cases one of the congenitally right handed subjects, who was left handed, admitted that he was closely associated with an uncle whom he admired and that this uncle was left handed. Of the three female subjects who were congenitally right handed and became left handed, one of them stated that she purposely trained herself to be left handed.

In order to further substantiate the validity of the hair whorl sign, a study was made of the hair whorl sign in 816 infants at birth and recorded the location of the hair whorl. The infants were repeatedly tested by objective tests depending upon the age, and the mothers were questioned in relation to the subjective tests. This procedure was continued through the fifth year. (Table III.) The questions were:

1. Which hand holds a rattle?
2. Which hand holds a spoon?
3. Which hand reaches for an object?
4. Which hand holds a pencil?
5. Which hand throws a ball?
6. Which foot moves first when kicking?
7. Which hand or foot is used to strike a cradle gym?

The results were tabulated as right, left, or both.

The objective tests were:

1. Which hand is used in writing?
2. Squeezing fingers. Which hand appears the stronger?
3. Throwing a ball. Which hand is used?
4. Pinch nose. Which hand is put up first?
5. Which foot kicks a ball?
6. Which foot moves first when infant kicks?
7. Ask to clasp his hand in front of body. Which thumb is on top?
8. Clap hands. Which hand does the clapping?

These results were recorded as right, left, or both extremities.

Of the 816 infants at birth, it was noted that 101 (12½ per cent) were congenitally right handed (left hair whorl); 564 infants (69 per cent) were congenitally left handed (right hair whorl); 93 (11½ per cent) were ambilateral (mid-line hair whorl); and 58 (7 per cent) were ambidextrous (double hair whorl). It is to be noted that there was a predominance of congenitally left handed children in this study. However, when this study was commenced particular attention was directed to this sign in the congenitally left handed children and thus quite a number of right handed children were not recorded.

The 101 infants, who were congenitally right handed at birth, showed at the end of the first year by subjective and objective tests, 92 (91 per cent) right handed, 6 (6 per cent) left handed, and 3 (3 per cent) used either hand. At the end of the second year 53 infants of the original group of 101 were re-tested. By subjective and objective tests 48 (90 per cent) were right handed, 2 (4 per cent) were left handed and 3 (6 per cent) used either hand. At the end of 5 years only 14 subjects of the original 53 tested at the end of the second year were

DIAGNOSIS FOR HANDEDNESS

BY HAIR WHORL SIGN (Congenital Handedness)			BY SUBJECTIVE AND OBJECTIVE TESTS								
			FIRST YEAR			SECOND YEAR			FIFTH YEAR		
RIGHT	No.	%	Right	Left	Both	Right	Left	Both	Right	Left	Both
Left hair whorl	101	12½	92 91%	6 6%	3 3%	48 90%	2 4%	3 6%	9 64%	4 29%	1 7%
LEFT											
Right hair whorl	564	69	11 2%	492 94%	22 4%	59 22%	129 48%	80 30%	33 30%	38 34%	41 36%
AMBILATERAL											
Mid-line hair whorl	93	11½	24 30%	14 18%	41 52%	18 43%	6 14%	18 43%	5 25%	1 5%	14 70%
AMBIDEXTROUS											
Double hair whorl	58	7	1 3%	7 16%	35 81%	5 31%	1 7%	10 62%	2 9%	1 4%	20 87%

TABLE III—RESULTS OF HAIR WHORL SIGN (CONGENITAL HANDEDNESS) AS COMPARED TO RESULTS OF HANDEDNESS BY SUBJECTIVE AND OBJECTIVE TESTS.

available for re-testing. By subjective and objective tests 9 (64 per cent) were right handed; 4 (29 per cent) were left handed, and one (7 per cent) used either hand.

Of the 564 infants who were congenitally left handed at birth, 525 infants were seen at the end of the first year. By subjective and objective tests 11 (2 per cent) were considered right handed; 492 (94 per cent) were considered left handed and 22 (4 per cent) used either hand. At the end of the second year 268 infants were available for re-testing. By subjective and objective tests 59 (22 per cent) were considered to be right handed; 129 (48 per cent) were considered to be left handed and 80 (30 per cent) employed either hand. At the end of the fifth year 112 subjects were re-tested. Subjective and objective tests showed that 33 (30 per cent) were considered right handed; 38 (34 per cent) were considered left handed and 41 (36 per cent) used either hand.

Of the original 93 subjects who were considered congenitally ambilateral, 79 were tested at the end of the first year. According to subjective and objective tests, 24 (30 per cent) were considered to be right handed; 14 (18 per cent were considered to be left handed and 41 (52 per cent) were able to use either hand fairly well. At the end of the second year 40 were retested. By objective and subjective tests 18 (43 per cent) were considered to be both, right and left handed. At the end of the fifth year, 20 were retested. Five (25 per cent) were considered to be right handed; one (5 per cent) was considered to be left handed; and 14 (70 per cent) were able to use either hand fairly well.

Fifty-eight infants (7 per cent) of the entire group were considered congenitally ambidextrous. At the end of the first year 43 infants were tested subjectively and objectively. One (3 per cent) was considered to be right handed; 7 (16 per cent) were considered left handed; and 35 (81 per cent) were considered both right and left handed. At the end of the second year 16 were retested. Five (31%) were considered right handed; one (7 per cent) was considered left handed and 10 (62 per cent) were considered to be both, right and left handed. At the end of five years, 23 subjects were re-examined by subjective and objective tests. Two (9 per cent) were considered to be right handed; one (4 per cent) was considered to be left handed; and 20 (87 per cent) used both hands well.

Analysis of Children's Data: It is readily seen that the congenitally right handed infants at the end of the first and second years were almost all right handed. For the fifth year determination there were too few congenitally right handed infants followed for statistical importance, but even in this small group, the congenitally right handed children were still predominantly right handed. In the congenitally left handed group, there is a gradual but definite decrease from left handedness by the end of the fifth year as compared to the first year. We believe the reason for this change is environmental and cultural. We learned that the majority of mothers of these congenitally left handed infants kept putting toys and eating utensils into the right hand or taking them out of the lef hand and puting them into the right. A number of parents did not realize what they were doing until their attention was called to the matter. However, a number of children at the end of the fifth year still resisted the change from left handedness to right handedness. In the congenitally right handed infants, six were considered left handed at the end of the first year. Three of these infants were born with Erb's paralysis of the right upper extremity requiring treatment by splints, and one infant had a fracture of the right humerus at birth. The remaining two were considered imitative—in both cases an older brother was left handed. Both imitative youngsters became right handed by the time they were five years of age. The congenitally ambilateral and congenitally ambidextrous children still showed 70 and 87 per cent respectively the same ambilaterality and ambidexterity on subjective and objective tests at the end of the fifth year. To account for this fact, we believe that the parents did not attempt to convert the infants to right handedness because of the infants' ability to use the right hand in eating and writing. The findings in the congenitally ambilateral and congenitally ambidextrous subjects agree with the conclusion of

Blau who claims preferred laterality begins to appear at about nine months of age but continues to develop through childhood and even later. In other words, the incidence of dextrality in children increases with age as they are exposed to more and more educational and cultural influences.

The location of the hair whorl remained constant in all the children tested.

Discussion

Since the hair whorl is located on different sides of the scalp, there must be a reason for this difference in location—the location of the hair whorl could indicate the natural handedness of the individual. Since language can be based on a cerebral dominance theory, why could not handedness also be based on cerebral dominance? Peterson[6] has shown on experimental work with the rat that dominance as to handedness is dependent on intact motor and somaesthetic fields in the opposite cerebral hemisphere. Eames[7] believes that the brain center controlling manual dominance is located in the prefrontal gyrus on the side opposite to the dominant hand. In congenital handedness the hair whorl can be considered to be located on the same side as the cerebral hemisphere which controls the opposite side of the body.

Cultural and environmental factors cause the marked predominance of right handed individuals in our civilization. Thus the discrepancy between the hair whorl sign and actual handedness in adult life is explained. It is noted that the error for the congenitally right handed individuals according to the hair whorl sign is negligible in adults when compared to subjective and objective tests for handedness. The error for the congenitally left handed, ambilateral, and ambidextrous in adults is in keeping with the accepted fact that right handedness is a cultural characteristic. Observation in children over many years plus the detailed study of 500 individuals from 5 to 70 years of age, has verified the validity of the hair whorl sign for congenital handedness.

We are not interested to determine whether parents should train their children to be right handed or permit them to develop their natural tendencies. If the latter course is pursued, then the location of the hair whorl will guide the physician in instructing the parents as to the congenital handedness of the child. Although the problem of aphasia is not definitely understood, the hair whorl sign may have some significance for those who are interested in the training of aphasics in relation to handedness. In rehabilitation programs the hair whorl sign may be used to advantage when retraining individuals to use other extremities, that is, an individual may be right handed due to cultural factors, yet he is congenitally left handed. Such an individual can be trained to become left handed much more quickly than one who is congenitally right handed.

Conclusion

1. Congenital handedness can be determined clinically by the hair whorl sign.
2. The location of the hair whorl remains constant.
3. Environmental training and cultural demands modify congenital left handedness, congenital ambilaterality, and congenital ambidexterity.
4. The practical applications of the hair whorl sign are indicated.

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Neurological Clinical Pathological Conference

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CHARLES D. ARING, M.D., *Editor*

CASE NO. 249077

Presentation

A 3-year-old white boy was admitted to the hospital for the second time, November 6, 1950, with complaints of vomiting for 2 days and nuchal pain for 3 days. He died December 16, 1950.

The patient had always been pale and of less than normal vigor, but no other obvious abnormalities of birth and development were recorded. The first admission to the hospital, October 2, 1950, followed an illness of 7 days beginning with abdominal distension and pain and vomiting without nausea. Vomiting and abdominal pain persisted, and for a period of two days the parents observed tarry stools but no other fecal abnormality was reported. The mother had noted several pin point spots on the abdomen which disappeared after 24 hours, but she did not describe purpura.

In the physical examination at the time of the first admission enlarged and inflamed tonsils and an inflamed pharynx were recorded. Eyes and nose were normal. The neck was supple and cervical nodes were not enlarged. The lungs were clear, respirations 35. The heart was not enlarged, the rhythm was regular, rate 140, and no murmurs were heard. The abdomen was moderately distended, the spleen palpable one finger-breadth, and the liver two finger-breadths below the costal margins. No other masses were felt and minimal peristalsis was heard. No lesions were seen on the skin and superficial nodes were not enlarged. Neurological examination was normal.

Blood studies in October 1950 showed: red cells, 3.7 million per cmm.; hemoglobin, 7.7 gm. per 100 cc.; hematocrit, 29 per cent; reticulocytes, 5 per cent; platelets, 391,650 per cmm.; mean corpuscular volume, 77 cubic microns; mean corpuscular hemoglobin, 20 micromicrograms; mean corpuscular hemoglobin concentration, 26 per cent. The sedimentation rate of erythrocytes was 17 mm. per hour. The white cell count was 8,450 per cmm. with 58 per cent neutrophils. (White cell count on admission was 20,000 with 70 per cent neutrophils.) Anisocytosis, poikilocytosis, and hypochromasia of red cells was observed. The urine gave negative tests for albumin and sugar but the sediment contained 10-15 white cells per high power field. Three stool specimens were guaiac negative. A Kahn test of the blood was negative. The prothrombin level was 85 per cent. Agglutinations for typhoid, brucella, paratyphoid, and heterophile antibodies were negative. A blood culture showed no growth, and a stool culture was negative for enteric pathogens. Negative reactions were obtained with tuberculin and histoplasmin.

Flat and upright films of the abdomen showed an absent psoas shadow on the right. Several fluid levels were seen in the region of the ascending colon. A chest film showed mild cardiac enlargement. Barium enema was normal.

Penicillin was administered and the patient improved. Temperature was 102.5° F. on October 4 and up to 100 thereafter. Episodes of profuse diaphoresis were recorded. The parents removed the child from the hospital October 11, 1950, against advice.

On November 1 he developed a mild upper respiratory infection and three days later complained of nuchal pain, held his head extended, and resisted examination of the neck. Vomiting recurred the following day and on the next day he refused all food and fluids but ice water.

Examination on November 6 revealed irritability and pallor but fair development. Cervical and inguinal nodes were palpable but not greatly enlarged. The head measured 55 cm. in circumference. Convergent strabismus was present; the pupils were equal with normal reaction. Light reflexes of the eardrums were thickened. No lesions were seen on the mucous membranes of the mouth or pharynx. The neck was not stiff and the trachea was in the midline. The lungs were clear; respirations were 20. The heart did not appear enlarged. Systolic murmurs were heard at the apical and pulmonic areas. The rhythm was regular, rate 100. Blood pressure was 110/80. Spleen and liver each were 3 finger-breadths below the costal margins. No other abdominal masses were felt. Reflexes were normal.

Studies by the Hematology Laboratory on November 8, 1950, showed: red cell count, 4.11 million per cmm.; hemoglobin, 8.5 per 100 cc.; hematocrit, 31 per cent reticulocytes, 8.9 per cent; platelets, 45,210 per cmm.; mean corpuscular volume, 75 cubic microns; mean corpuscular hemoglobin, 20 micromicrograms; mean corpuscular hemoglobin concentration, 26 per cent; white cell count, 12,250 per cmm. with 65 per cent neutrophils. A test for sickling was negative. A stained film showed similar changes in the red cells as noted previously and platelets were described as abundant. A repeated Kahn test of the blood was negative. A Coombs test was negative. A negative urine was obtained. Negative guaiac tests of the stools were found on several occasions but two were positive. Blood protein was 6.2 gm. per cent with 4.0 gm. albumin. A liver profile showed: thymol turbidity, 12 units; zinc sulfate turbidity, 18 units; cephalin flocculation, negative in 24 hours; total lipid, above 1500 mg. per cent; serum bilirubin, 0.15/1.9 mg. per

cent; alkaline phosphatase, 4 units per cent. There was little change in these values six days later. Blood cholesterol was 170 mg. per cent. Fasting blood was 63 mg. per cent and blood urea nitrogen 22 mg. per cent. Repeated agglutinations were negative. Stool specimens were negative for ova and parasites, and cultures did not show pathogenic organisms. Marrow aspirated from the ilium revealed erythroid hyperplasia, principally at the normoblastic level. Skin tests with tuberculin, histoplasmin and trichinella antigen were negative.

Normal upper gastro-enteric series and small bowel study were obtained. Fluoroscopy of the heart showed cardiac enlargement, predominantly left ventricular. Films of the long bones showed lines of increased density of the epiphyseal plates of fairly marked degree. Skull films on November 9, 1950, were normal, but on December 15 showed slight separation of the coronal and sagittal sutures. Mastoid films were normal.

Vomiting abated but the patient had periods of irritability and poor appetite. On November 26 it was recorded that the liver and spleen had diminished considerably in size. Feosol was begun November 30. On December 1 esophagoscopy was negtive and discharge was contemplated. During this period temperatures between 99° and 100° were recorded almost daily. A hiatus in the clinical record between December 2 and December 14 is covered by the nursing notes. In this period the patient received Feosol, had a variable appetite, and showed periods of irritability. Early on the morning of December 13 he coughed severely and vomited a large amount of undigested food, and vomiting persisted at intervals during the next two days. At 8 P.M., December 14, he had repeated tonic and clonic convulsions. Absent left abdominal skin reflexes and unsustained left ankle clonus were observed. Seizures continued throughout the morning of December 15, each lasting up to 5 minutes; they became confined to the right side, and he was stuporous between seizures. Kernig and Brudzinski signs were negative and the neck was not rigid. In the afternoon he became worse. He continued to move the right arm but the left arm and leg were held in spastic flexion. Right internal strabismus and early papilledema appeared. A lumbar puncture revealed a pressure of 600 mm. of water. The fluid was clear and contained 3 lymphocytes per cmm. Later in the afternoon the retinal veins became distended, the color of the fundi became dark red, and the pulse rate fell to 60. Bilateral subtemporal decompression was performed at 6:50 P.M. On opening the dura on each side there occurred great herniation of the temporal lobes with rupture of brain substance. Right-sided seizures continued during the operation and were combated with anti-convulsants, but respiratory distress developed. He was returned to the ward in a perilous state, temperature 104°, pulse 160, and respirations 80. Right-sided convulsions continued in spasms lasting 20 minutes. He died at 9:15 A.M., December 16, 1950.

Differential Diagnosis

*Dr. Clark D. West**: This patient had a relatively long history dating back about 12 weeks prior to death. On both hospital admissions he presented a diagnostic problem. Preceding the first admission on October 2, he had an illness of one week's duration characterized by symptoms referable to the abdomen. There was moderate distention, vomiting (which was described as not preceded by nausea), abdominal pain, and an episode of tarry stools. The child on admission was pale, listless, somewhat under size for his age of 3 years, appearing chronically ill, but not greatly debilitated. On physical examination there was evidence of acute infection in the throat, but the main findings were confined to the abdomen. The liver and spleen were easily palpable, but were not greatly enlarged, the abdomen was moderately distended, and audible peristalsis was minimal. On this first admission, attention was perhaps initially directed toward disease of the bowel—appendicitis, diverticulitis involving the colon, infiammation of a Meckel's diverticulum, volvulus, or intussusception—but on closer study these conditions may be dismissed. After an illness of a week's duration, an acute process in the bowel usually results in peritonitis, and peritonitis in young children is usually diffuse rather than local, possibly due to the relatively small omentum. The moderate abdominal distention, the failure of the protocol to mention abdominal tenderness, the absence of constipation, and the absence of signs of sepsis and dehydration make peritonitis, whether it be diffuse or local, unlikely.

Disease of the kidney or of the perirenal structures may be considered. As you know, pyelonephritis may simulate disease of the bowel and is suggested by the mild pyuria. Pyelonephritis, however, is about six times more common in females than males, and usually at some time in the course the patient is septic and febrile. This patient was not. The absence of a psoas shadow by x-ray points to a perinephric abscess or even to a local peritoneal infection, but when considered logically, sufficient edema to obscure

*Assistant Professor of Pediatrics.

the psoas shadow should be present only when there is a considerable inflammation, and there should be signs of psoas spasm demonstrable on manipulation of the legs, or indicated by a characteristic position chosen by the child. These signs were absent, and one tends to put little weight on the absence of the psoas shadow.

The tarry stools and the pin-point spots on the abdomen might point to a primary hematologic disorder. A moderately severe hypochromic, microcytic anemia is present and the 5 per cent reticulocyte count gives evidence of blood regeneration. The rest of the blood picture is normal. This evidence does not support the diagnosis of leukemia; and the diagnosis of purpura is not indicated by the hospital course.

Studies and observations of this child were interrupted by the parent's insistence that he be returned home, and it would appear from the protocol that the attending physicians had not as yet reached a diagnosis. As a last backward look at this first admission, it might have been better to place more emphasis on the story of vomiting without nausea, as indicating a reflex vomiting, perhaps of central nervous system origin, which produced secondarily the signs in the abdomen.

The child was returned to the hospital after 3 weeks at home with signs and symptoms which seem to justify somewhat our suspicions of a central nervous system lesion. This time there was headache localized to the back of the head and neck. There was recurrence of vomiting. The child preferred to lie with his head extended. He was irritable, and had strabismus. The head measured 55 cm. which is about 5 cm. too large for his age, but in view of the roentgen findings that suture separation was absent at this time, one might suspect that this is simply a normal variation. The overall picture is still not clear, and central nervous system disease apparently was not seriously considered, at least not enough so that a lumbar puncture or a funduscopic examination was performed. Instead, the further enlargement of the abdomen and the anemia attracted attention. The anemia was still present to the same degree as previously, 8.5 gm. per 100 cc. It was hypochromic and microcytic, and now the reticulocytes have increased to 9 per cent. The protocol is a little confusing as to platelets. They are reported as 45,000 in the count, but on stained smear were reported as abundant. At least we know there was no bleeding tendency on this admission. The bone marrow which showed only erythroid hyperplasia verified the peripheral blood picture, and a blood dyscrasia seems unlikely. The cardiac enlargement and the murmurs may be explained on the basis of the anemia, but the enlargement of the liver and spleen is puzzling. The bilirubin was increased, but not enough to produce jaundice. It was 1.9 mg. per cent and was predominantly indirect in reaction which would indicate a hemolytic process rather than primary liver disease. The liver profile studies also did not point to primary liver disease. The total lipids were markedly elevated, about double the normal value. I don't know how this helps in arriving at a diagnosis. The thymol turbidity was increased as was the zinc sulfate, but apparently these deviations from normal may be attributed to the abnormality in the blood fat rather than to an abnormality in the gamma globulin fraction.

There is one disease which is found both in adults and in children in which the hepatomegalia and splenomegalia occur in conjunction with anemia and thrombocytopenia, and this is Banti's disease or congestive splenomegaly. In one form of this disease there may be esophageal varicels which may rupture and can produce hematemesis, and hematemesis is one of the common presenting symptoms. Apparently this disease was considered since an esophagoscopy was done and no varices were found. The absence of varices does not rule out Banti's disease, but makes it quite unlikely.

It would be well to return to the possibility that there is a central nervous system lesion. One would have to pick an entity which is associated with systemic signs, particularly with anemia. Thus brain tumor or brain abscess would seem unlikely. On the other hand, a tumor elsewhere in the body with metastases to the brain would be a good prospect. By far the most common of these is a neuroblastoma. This tumor usually arises in the adrenal gland and metastasizes to liver, bones, and brain. This diagnosis

would explain the hepatic enlargement, the central nervous system symptoms, and the anemia, but we have no evidence of any primary lesion. In sympathicoblastoma of this long duration, one usually feels a mass or sees calcification in the perirenal area by x-ray. Involvement of the liver and brain without boney metastases is also unusual with sympathicoblastoma.

One of the roentgen observations on this admission is of interest, and I am speaking of the increased density at the epiphyseal plates of the long bones.

Dr. Benjamin Felson (demonstrating x-rays): Here's one of the earlier films from the first admission, the film on which the right psoas shadow could not be demonstrated. I think you can faintly see the left psoas, but the right one is not visualized despite the absence of gas. The absence of psoas shadow on one or several films is common in normal people, so alone it is not a completely reliable sign. The heart on the first examination showed an increase in transverse diameter of moderate degree, and this was confirmed fluoroscopically. Here is a left oblique view, nearly a lateral view, showing the heart almost overlapping the spine. So, there is posterior enlargement which we attributed to probable left-sided enlargement.

Here is the first skull film on the second admission, and we see the normal suture lines throughout and no other abnormalities, in contra-distinction to the next film made 3 to 4 weeks later which shows a distinct separation of the suture lines.

Finally, we have the appearance of increased density at the ends of long bones which is rather striking. This is seen on all the bones that grow rapidly, that is, all the bones around the knee joint, around the ankle, and even in the bones of the feet on other films. Here is the forearm. You will note the same process and that the metacarpals do show a suggestion of it. It is not seen around the elbow since these bones grow less rapidly than others.

Dr. West: The lines at the epiphyseal plate that you just saw were striking. When lines such as this are observed roentgenographically one should always consider lead poisoning, but it should be pointed out that such lines may occur in other conditions. They are not diagnostic of lead poisoning but are a great aid in confirming that diagnosis. They may appear during or following any illness sufficiently severe to arrest growth for some time. In this case, lead poisoning well fits the picture of a disease with central nervous system and systemic manifestations. In children the systemic symptoms of lead poisoning consist of anemia with reticulocytosis, pallor, which has been described as out of proportion to the degree of anemia, vomiting, abdominal pain, and headache. All of these were present in this child. In a child with lead stored in the body, symptoms of poisoning are often precipitated by mild acute infection. That was the case here on both admissions. Lead does not as a rule produce hepato or splenomegaly, and it might be hazarded that the enlargement of these organs was on the basis of extramedullary hematopoiesis resulting from the long-standing anemia. Basophilic stippling was not described but it should be pointed out that it is usually not seen unless it is specifically looked for. There was no history of lead ingestion, but again this information often has to be wheedled out of the parents. Often they are not aware of the danger of abnormal eating habits in their children. A record of the blood lead level, which is essential for confirming the diagnosis, is absent from the protocol. I wonder if I might ask what the blood lead level was and when it was done?

Dr. William T. Collins: It was 0.15 mg. per cent.

Dr. West: 0.15 mg. per cent is a considerable elevation of blood lead. The level at which signs of toxicity may be manifested is 0.06 or 0.08.

The final hospital course in this case is typical of lead encephalopathy, a condition characterized by progressive and severe cerebral edema. The child remained irritable, vomiting recurred, there was generalized convulsions, and he became stuporous. There were obvious signs of increased intracranial pressure. The description of the bitemporal decompression, which was performed as a last resort, allows one to picture a massive edema of the brain substance. There was herniation of the temporal lobes and frac-

ture of the brain substance exuding through the incision.

The final diagnosis and the cause of death may be stated with some certainty in this case as chronic lead poisoning and the cause of death, lead encephalopathy.

*Dr. A. A. Weech**: I think we'd all be interested in knowing what the impression was at the end of the first hospital admission.

Dr. Hugo Smith: Studies were being conducted to try to determine the cause of gastro-enteric bleeding. He was to have had a barium enema and a gastro-enteric series, when the parents took him home. On readmission Banti's syndrome was discussed in the first Pediatric Conference.

Dr. Richard Vilter: I attended this Pediatric Conference. This child had an enlarged liver and spleen, a microcytic hypochromic anemia, and there was the story of bleeding from the gastro-enteric tract. He was considered at the time to have anemia due to chronic blood loss, and the possibility of Banti's syndrome was considered.

Dr. William T. Collins: I believe that the tarry stools in this case are not due to blood but to lead sulphide which gives a similar appearance.

Dr. Weech: Hemorrhages in the fundi are a common symptom of lead poisoning; I don't believe hemorrhage in the bowel is.

Dr. John Mueller: I think there may be a typographical error concerning the platelet count because with the method we use we don't get within ten's as given in the protocol (45,210). The count was more likely 452,100.

*Dr. Ralph J. Johansmann:** The final diagnosis on this case is lead encephalopathy, Grossly, the most striking departures from normal were found in the brain. The brain weighed 1425 grams which is about 300 grams above the average for his age. It was pale, swollen, and there was flattening of the surfaces of the convulutions. There were two defects in the brain over the temporal lobes, each measuring about 3 x 4 cm. In these areas the brain tissue was softened and spotted with petechial hemorrhage; these areas were located deep to the sites of decompression. Otherwise, the brain showed edema. On sectioning, the ventricles were markedly compressed because of the edema. There was no softening of other portions of the brain, nor were there other petechial hemorrhages. The lungs were moderately increased in weight, subcrepitant, markedly congested, particularly in the lower lobes where there was also a small amount of pneumonia present. The heart was dilated, and the myocardium was pale and flabby. The abdominal viscera were moderately congested. The liver was slightly enlarged, and the spleen was moderately enlarged, being about 1½ times the normal weight.

Analysis of tissues for lead by the Kettering Laboratory* revealed that the brain contained 0.265 mg. of lead per 100 grams (usual values run from 0.01 to 0.1). The lead concentration in this brain was about 2½ times the highest acceptable value. The lead content of the liver was moderately increased; it was 2.05 mg. per 100 grams, and the upper limit of normal is 0.9.

Microscopic sections from the cerebral hemisphere showed marked edema of the tissues. The perivascular spaces were dilated, and there were clear areas around many of the cells, an edematous change. There was some precipitation of protein in some of these perivascular spaces, a finding seen in lead encephalopathy.

In the cortex there was extensive degeneration of nerve cells. Many of the nerve cells were shrunken and the nuclei pyknotic. With the neuronal degeneration there was some proliferation of endothelial cells of capillaries; this has been described in lead encephalopathy though it is not pathognomic. The finding of a high concentration of lead in this brain allows us to presume that the endothelial proliferation is an accompaniment of lead encephalopathy.

Sections of lung showed an accumulation of inflammatory cells around the wall, and here and there some exudation into alveolar spaces, an acute bronchitis; and a slight amount of lobular pneumonia. In addition, there was a moderate degree of pulmonary

*Professor of Pediatrics.
*Assistant Professor of Pathology.

*Kettering Laboratory of Applied Physiology.

congestion; many alveoli were filled with fluid.

The bones showed a characteristic lesion of lead deposition. Before showing the bone from this case, I want to demonstrate a section of normal bone. The bone from a child about the same age who died within a 24-hour period of meningococcemia shows normal costochondral junction. As you will recall, in intracondylar bone formation there is a zone of resting cartilage cells and a zone of proliferating cartilage cells. These cartilage cells line up into columns, more or less parallel to one another. The matrix between these cells become permeated with calcium salts, and, as the blood vessels invade this cartilage, the calcified matrix stands out as the primary trabeculae. It is on the surfaces of these primary calcified trabeculae that the osteoblasts deposit. Osteoid tissue then becomes calcified.

The next section is taken from the costochrondal junction of this child, and one immediately sees the difference. The cartilage is normal. There is a resting zone and a proliferating zone. There is a zone of the primary calcified trabeculae of the bone, and this is the zone which you saw in the x-ray film. Cartilage cells are lining up here as they did in the normal section, and these degenerating cartilage cells are being penetrated by blood vessels from the shaft. However, you notice that these primary trabeculae are permeated with calcium salts and they also become permeated with lead salts extending deeply into the shaft. You also notice that they are much increased in number. You do not see them disappearing here at the line of ossification as they did in the normal, but they persist, and practically every one of these trabeculae can be followed down toward the bone. In addition, there are a number of osteoblasts in the marrow spaces, multinucleated cells. The latter are not too well understood. Pathologists think that they represent futile attempts at removal of this calcified and solidified matrix, frustrated osteoblasts, but the biochemists have different ideas. This is the zone one sees in x-ray which is permeated with lead which for some reason or other is quite stable and is not removed in the normal process of remodeling of the bone. One sees even in these deep trabeculae, which are covered with osteoid tissue, some of these trabeculae which remain in the same group.

The next section is similar. It was taken from the femur. Here again one sees this broad film of trabeculae which represented the lead line on x-ray. It is not only the presence of lead in this matrix, but it is the increased number of these trabeculae which give the shadow.

Clinical Diagnosis

Lead poisoning.

Dr. West's Diagnosis

Chronic lead poisoning.
Lead encephalopathy.

Anatomical Diagnosis

Lead poisoning.
Lead encephalopathy.
Lobular pneumonia.
Acute bronchitis.

Dr. M. A. Blankenhorn: What was the mechanism of the swelling?

Dr. Johansmann: That's a good question. Theoretically it is felt that lead interferes with cell respiration enzyme systems, and decreased oxygen uptake is the result.

Dr. Morris W. Dexter: How specific is stippling in heavy metal poisoning?

Dr. Vilter: The gross basophilic stipplings doesn't mean very much, but the fine dust-like stippling is pretty specific.

Student: Since the age group in which lead intoxication occurs is usually younger or older, I wonder if any attempt was made to trace the source of the lead?

Dr. Hugo Smith: No source of lead was found.

Student: What is the typical age group?

Dr. Smith: Usually 18 months or younger. They are just old enough to get up and stand on the side of the crib or to reach the window still. As to the incidence, from 1941 through 1951 we have had 40 cases. So far in 1951* there have been 17 cases with 6 deaths. Of the 40 cases there are 9 who may not have had encephalopathy as far as we could tell, and 7 of those 9 had vomiting as one of their symptoms. These 9 did not have the usual findings associated with encephalopathy, and they did not have in-

*As of November 8, 1951.

creased intracranial pressure. It may well be that mild cerebral edema was present that we could not pick up.

Dr. Blankenhorn: Was there any period in the first admission when therapy with BAL might have been effective?

Dr. Smith: Quoting Dr. Robert Kehoe's experimental work with adults, BAL lowers the blood level with relative rapidity, in a matter of hours. There occur relatively insignificant changes as far as he can tell in the tissue lead in adults, and there has been essentially no change in the course of the illness with the use of BAL. In contrast, a group at Johns Hopkins reported in 1950 that BAL may have contributed to lowering of mortality and of the severe complications. I understand that they have become less enthusiastic with the passing of time.

Dr. Felson: How do you explain the increased incidence in the past year over earlier years?

Dr. Smith: I'm sure that improved diagnostic acumen doesn't contribute very much. While the hazard of lead paints no longer exists as such since the white lead has been removed, lead has reappeared in painting in the form of fixers and also in various plastic elements. Perhaps educating the public, which had been discontinued, needs to go forward again.

Dr. Weech: The evidence suggests that these children even when they do recover make a poor adjustment to life later on. Dr. Kehoe feels that the amount of lead removed by BAL is insignficant in terms of the total amount stored in the body. Some of us wonder even so if BAL therapy shouldn't be undertaken over longer periods of time in a manner that it hasn't been used heretofore in an attempt to de-lead these patients and attempt to prevent these unfortunate sequelae.

Dr. S. A. Trufant: I'd like to make one point in the absence of the neurosurgeons. In cases such as this, where in doing temporal decompression the brain herniates and disintegrates upon the boney margins, they are now attempting to handle this by using a small twist-drill hole and a catheter as a less traumatic method of decompression. It is felt that the result with this technique of decompression—because there's no question that these children have to be decompressed—is much more satisfactory.

Dr. Vilter: How is the swelling of the liver and spleen explained?

Dr. Johansmann: I failed to mention that there was a moderate degree of fat infiltration in the liver. In the spleen there was congestion and foci of extramedullary hematopoiesis which were small.

Dr. Edward Gall: Was the splenomegaly striking?

Dr. Johansmann: It was not too striking at the time of autopsy. It had been at one time during the clinical course.

Student: Does lead produce hepatitis? In the old literature there are numerous references to lead hepatitis with jaundice, and some authors even went so far as to say that every case of lead poisoning presented with jaundice; I didn't see any references to it in modern texts.

Dr. Johansmann: I think our experience with it has been that it does not produce hepatitis. There has been minimal change in the liver. Sometimes we find slight degeneration of liver cells.

Dr. Gall: Would you comment on the presence of inclusions in cases of this nature.

Dr. Johansmann: There have been noted intranuclear inclusions in the hepatic cells. These inclusions are acid fast. They have also been noted in the epithelial cells of the kidney. They are not pathognomic of lead intoxication; they are seen also with other heavy metals. This case had a few indefinite inclusions in a few of the hepatic cells. However, these were not acid fast, and I don't know what they mean. They are probably just degenerative products of the nuclei.

Student: How much paint does a child have to eat before he gets sick?

Dr. Smith: I don't know the exact figure; Dr. Kehoe probably could give relatively exact amounts. There are two factors that are important in producing lead poisoning. One is the duration of the exposure and the other is the amount per diem. Chronic mild exposure can produce lead poisoning just as readily as short rapid exposure. Those children who inhale lead fumes from burning lead battery boxes get it rapidly and have had far less exposure to lead than those who absorb it through the intestinal tract.

Dr. Felson: Are any of them from ingesting plaster rather than paint?

Dr. Smith: Plaster per se is free of lead. Putty contains lead, but many plasters have a lot of old paint on the surface.

Student: Was any renal pathology noted in this case?

Dr. Johansmann: None.

Dr. Gall: What is your experience with marrow aplasia in lead poisoning?

Dr. Johansmann: I don't believe it's a common occurrence.

Dr. George Guest: The anemia associated with lead poisoning at this age period is as a rule primarily the result of iron deficiency, a concomitant circumstance rather than any causal relationship between the lead and the anemia.

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